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● *Original Contribution*

A NEW METHOD FOR DISCRIMINATING BETWEEN BRONCHIAL AND PULMONARY ARTERIAL PHASES USING CONTRAST-ENHANCED ULTRASOUND

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Abstract—This study aimed to explore the value of a real-time comparative observation method using contrast-enhanced ultrasound (CEUS) for discriminating between bronchial and pulmonary arterial phases in diagnosing lung diseases. Forty-nine patients with 50 pulmonary lesions (45 peripheral lesions and five central lesions with obstructive atelectasis, including 36 malignant tumors, five tuberculomas, four inflammatory pseudotumors and five pneumonia lesions) detected *via* computed tomography and visible on ultrasonography were enrolled in this study. The arterial phases were determined by comparing contrast agent arrival time (AT) in the peripheral lung lesion with that in adjacent lung tissue, referred to as a real-time comparative observation method. Detection rates of this observation method were 100% (50/50) for pulmonary arterial phase and 88% (44/50) for bronchial arterial phase. Using the instrument's built-in graphing and analysis software, a time-intensity curve was constructed based on a chosen region of interest within the lesion where enhancement was the most obvious. Commonly used perfusion indicators in CEUS, such as AT, time-to-peak and peak intensity, were obtained from the time-intensity curve. Percutaneous puncture biopsies were performed under ultrasound guidance, and specimens of all 50 lesions were examined pathologically. AT was significantly shorter in patients with pneumonia than in those with malignant tumors or chronic inflammation ($p < 0.05$), whereas no difference was seen between those with malignant tumors and those with chronic inflammation. No significant differences in time-to-peak or peak intensity were seen among those with various lung diseases ($p > 0.05$). This is the first description of a real-time comparative observation method using CEUS for determining the arterial phases in the lungs. This method is accurate, simple to perform and provides a direct display. It is expected to become a practical and feasible tool for diagnosing lung diseases. (E-mail: 168hewen@sina.com) **© 2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Ultrasound, Contrast-enhanced Ultrasound, Pulmonary, Biopsy.**

INTRODUCTION

Contrast-enhanced ultrasound (CEUS) can be used to evaluate microcirculation perfusion in organs and tissue and is widely used in diagnosing multiple organ diseases. However, because ultrasound cannot be used to visualize gas-containing pulmonary tissue, application of CEUS in lung diseases has been limited. In recent years, researchers have attempted to utilize CEUS in diagnosing peripheral pulmonary lesions that can be visualized on ultrasound, with some success (Görg et al. 2005, 2006a, 2006b, 2007; Qureshi et al. 2011; Sartori et al. 2013). With regard to related perfusion indicators, the importance of arrival time (AT) in the lungs has been recognized (Caremani et al. 2008; Görg et al. 2006b, 2006c; Piscaglia et al. 2012; Qureshi et al. 2011). However, AT might be influenced by injection speed of the contrast agent and/or cardiac output of the patient (Piscaglia et al. 2012). In addition, the interval between pulmonary and bronchial arterial phases is only a few seconds; thus, defining the arterial phases solely on the AT in lesions might result in errors in diagnosis and subsequent treatment (Caremani et al. 2008; Görg et al. 2006b, 2006c; Piscaglia et al. 2012; Qureshi et al. 2011). In this study, we aimed to explore the value of a new method using CEUS for discriminating between bronchial and pulmonary arterial phases in order to

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solve the inherent problems in the existing methods used for diagnosing lung diseases.

MATERIALS AND METHODS

Forty-nine patients with 50 pulmonary lesions (45 peripheral lesions and five central lesions with obstructive atelectasis, including 36 malignant tumors, five tuberculomas, four inflammatory pseudotumors and five pneumonia lesions) detected *via* computed tomography and visible on ultrasonography were enrolled in this study. The patients included 31 men and 18 women with a mean age of 64.8 ± 12.5 y.

The GE Logiq E9 color Doppler ultrasound system equipped with a 2–4 MHz convex array probe (GE Company, Fairfield, CT, USA) was used. Conventional ultrasound was employed to observe the size, morphology, internal echoes and color Doppler flow images of the lesions. All 50 lesions were examined by using low–mechanical index CEUS. Of the 49 patients, seven were examined twice (six with unsatisfactory images due to tachypnea or cough during examination, one with two lesions) and the others only once. The contrast agent used was SonoVue (Bracco Imaging, Milan, Italy), a second-generation ultrasound contrast agent. Lyophilized contrast agent was suspended in 5 mL physiologic saline solution. At each time point, 2.4 mL of contrast agent suspension were injected into the cubital vein, followed by injection of 5.0 mL saline solution as a flush. The interval between two injections of contrast agent was at least 10 min.

The arterial phases were determined by comparing ATs of contrast agent in the peripheral lung lesion with that in adjacent lung tissue, referred to as a real-time comparative observation method. The moment when microbubbles appeared within gas-containing pulmonary tissue adjacent to the lesion was deemed as the start of the pulmonary arterial phase. The moment when microbubbles appeared within the lesion was deemed as the start of the bronchial arterial phase (Fig. 1). Lesions that enhanced simultaneously were deemed to be receiving blood supply from the pulmonary arteries, whereas those that enhanced after a delay of a few seconds were deemed to be receiving blood supply from the bronchial arteries.

Using the instrument's built-in graphing and analysis software, a time-intensity curve (TIC) was constructed based on a chosen region of interest within the lesion where enhancement was the most obvious. Commonly used perfusion indicators in CEUS, including AT, time-to-peak (TP) and peak intensity (PI), were obtained from the TIC for statistical analysis. To offset the impact of different baseline intensities before contrast injection, PI was calculated as the difference between maximum and minimum intensities (Dietrich et al. 2012). Perfusion indicators were acquired from dynamic images stored by two senior sonographers who were blinded to the histologic findings of the lesions, and who reached a consensus on related issues.

Percutaneous puncture biopsies were performed under ultrasound guidance, cautiously avoiding the non-enhanced necrotic regions visualized on CEUS, and specimens of all 50 lesions were examined pathologically.

Perfusion indicators in the lesions were expressed as mean ± standard deviation (SD), and were analyzed statistically by using SPSS version 13.0 software (SPSS Inc., Chicago, IL, USA). Analysis of variance was performed to evaluate the significance of the quantitative indicators, with p values < 0.05 used to indicate statistical significance. This study was approved by our local ethics committee and written informed consent was obtained from each patient before the CEUS and biopsy procedures.

RESULTS

The mean size of the 50 lesions was 3.5 ± 1.3 cm, and the mean number of punctures was three (range, 1–4). Of all 50 lesions, 48 were diagnosed according to puncture biopsy specimens and the other two according to surgical and pathologic findings (including one malignant mesothelioma and one inflammatory pseudotumor). Thus, the confirmed diagnosis rate by using percutaneous puncture biopsy was 96.0% (48/50). Hemoptysis and pneumothorax occurred in one case each. The histopathologic results of all 50 lesions were as follows: 36 malignant tumors (including 13 squamous cell carcinomas, nine adenocarcinomas, four bronchoalveolar carcinomas, four small cell carcinomas, three metastatic cancers, two poorly differentiated cancers and one malignant mesothelioma), five tuberculomas, four inflammatory pseudotumors and five pneumonia lesions.

Using a real-time comparative observation method, the starts of pulmonary and bronchial arterial phases were 6.4 ± 1.0 s (range, 4.5–12.0 s) and 10.7 ± 1.8 s (range, 8.–17.0 s), respectively; the start time difference between the two arterial phases was within a range of 3.0–6.0 s. All lesions in the pneumonia group were enhanced in the pulmonary arterial phase, whereas all lesions in the chronic inflammation group were enhanced in the bronchial arterial phase. In the malignant tumor group, three lesions displayed slight periphery enhancement in the pulmonary arterial phase and marked central enhancement in the bronchial arterial phase; the other 33 lesions displayed enhancement in the bronchial arterial phase (Figs. 2 and 3). Of all 50 lesions, the start of the bronchial arterial phase was indiscernible in six lesions, including five pneumonia lesions and one central pulmonary carcinoma. Detection rates were 100%